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EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/019,067	PAULSSON ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-16 and 26-32* is/are pending in the application.

4a) Of the above claim(s) *15,16 and 26-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 14 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed May 4, 2007 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 32 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification on page 2, lines 5-9 discloses that is was an object of the invention to provide an improved assay for gluten sensitive enteropathies and in particular an antibody binding assay which allows a differential diagnosis of autoimmune diseases of the GSE-type, autoimmune disease associated with GSE and seemingly non-active latent gluten sensitive enteropathies. The specification on page 2, line 29 – page 3, line 26 disclose diagnosing a disease and at page 3, lines 25-26 discloses distinguishing autoimmune disease. Further, as indicated by Web definition under Goggle differential diagnosis is the determination of which two or more diseases with similar symptoms is the one from which a patient is suffering, based on an analysis of clinical data. The specification does not disclose the diagnosis of a second

autoimmune disease as currently recited. There is no description in the specification diagnosing a second autoimmune disease as recited.

3. Claims 13, 14 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing gluten sensitive enteropathy by testing a sample for IgA antibodies directed against human tissue transglutaminase and one other transglutaminase molecule selected from the group consisting of FXIIIA, TGk, TGx, TGe and Band 4.2 and correlating significantly increased amounts of the IgA antibodies concentrations of the sample as compared to a control sample with a diagnosis of gluten sensitive enteropathy, does not reasonably provide enablement for the mere presence or decreased amounts of IgA antibodies for diagnosing gluten sensitive enteropathy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for diagnosing autoimmune disease comprising taking a sample from a patient and testing the sample for IgA antibodies against human tissue transglutaminase and at least one other tranglutaminase molecule, wherein the presence of IgA antibodies in the sample is indicative of the existence of a gluten sensitive enteropathic autoimmune disease.

The specification on page 11, lines 18-20 discloses that control samples from healthy individuals and from patients suffering from disease that does clearly not have an autoimmune component are used in the assays as compared to other tested subjects. The specification on page 14, lines 10-22 disclose that the median antibody concentration for patients with untreated GSE was 61.4 AU, for controls 12 AU. Figure 3 of the specification discloses that the control patients which do not have autoimmune disease clearly have the presence of IgA antibodies against human tissue transglutaminase. The specification does not show the mere detection or presence of IgA antibodies against human tissue transglutaminase or decreases of IgA antibodies against human tissue transglutaminase are diagnostic of autoimmune disease or gluten sensitive enteropathy. Further, Locke et al (J . Clinical Pathology, 1999; 52:274-277) teaches that tissue transglutaminase is a major autoantigen in celiac disease, and teaches that IgA anti-tissue transglutaminase is closely associated with celiac disease in high titres but that low titres may not be disease specific. However, the prior art does not indicate the mere presence or decreased levels for diagnosing. The working examples and figures are limited to situations showing increased levels of diseased patients compared to patients lacking the disease. At best the diagnosis of gluten sensitive enteropathy can only be determined by the indication of significantly increased levels of IgA compared to that of

patients lacking the disease and correlating the results to a diagnose of gluten sensitive enteropathy. Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to diagnose gluten sensitive enteropathy, one skilled in the art would have to have a high level of predictability, in order to successfully diagnose the disease, and one cannot diagnose gluten sensitive enteropathy in which the mere presence or a decrease of IgA antibodies is detected without guidance or predictability.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is vague and indefinite because claim 13 is directed to diagnosing an autoimmune disease by detecting the presence of IgA antibodies against tissue transglutaminase and at lease one other transglutaminase molecule as recited, and it is unclear how determining both for diagnosing a gluten sensitive enteropathic autoimmune disease also diagnoses a second disease at the same time. How could one positively diagnose a disease when the markers (IgA) antibodies would also be know to be present in a second different disease? How would one differentiate between the two diseases? Further, it is unclear if applicant is actually trying to diagnose two different diseases at the same time or if applicant intends to somehow try and differentiate between the two diseases. Further, it is unclear how it is indicative.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 13 and 32 are rejected under 35 U.S.C. 102(b) or (e) as being anticipated by Schuppan et al (WO 98/03873 or US 6,319,726).

The WO and US references have the same disclosure. Schuppan et al disclose methods of detecting antibodies from body fluids by means of an immune reaction with tissue tranglutaminase (see '726 abstract). Schuppan et al disclose that the tissue transglutaminase can be human tissue transglutaminase (see '726, col 6, lines 20-22). Schuppan et al disclose that the tissue tranglutaminase can be immobilized and used to detected antibodies in a sample for diagnosing celiac disease (see '726, col 3). Schuppan et al disclose that the method is used to detect IgA antibodies.

With respect to the recitation "and at least one other transglutaminase molecule selected from FXIIIA, TGk, TGx, TGe and Band 4.2". Schuppan et al disclose that the antibodies to be detected are IgA antibodies which are against human tissue transglutaminase. These antibodies to be detected are the same as the antibodies detected by applicant (see specification). Thus, the antibodies of Schuppan et al would

be cross reactive with other antigens and would inherently be against TGe. As shown by Applicant the IgA antibodies are cross reactive . The specification on page 15 discloses "the results shown support that serum IgA antibodies from patients with CD and DH react with both human TGc and TGe and further discloses that the serum antibodies from patients with CD and DH is directed against epitopes which are shared by the two transglutaminases". Thus, it is inherent that the IgA antibodies of Schuppan et al are against both human tissue transglutaminase and TGe. Further, as stated above the body of the claim merely requires a step of taking a sample and testing the sample for IgA antibodies against human tissue transglutaminase and at least one other transglutaminase molecule. Thus, for the above stated reasons Schuppan et al reads on the instantly recited claim.

Also, regarding the interpretive "wherein" and "thereby" clauses as recited in the claims ("...wherein the presence of IgA antibodies in the sample is indicative of the existence of a gluten sensitive enteropathic autoimmune disease, thereby diagnosing an autoimmune disease"(as recited in claim 13) and (...wherein the presence of IgA antibodies against at least one other transglutaminase molecule") (as recitation as recited in claim 32): the clauses do not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps. Therefore, the "wherein" "thereby" clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See Texas Instruments, Inc. v. International Trade Comm., 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) ("A whereby clause that merely states the result of the

limitations in the claim adds nothing to the patentability or substance of the claim."). See also Minton v. National Assoc. of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) ("A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.").

Response to Arguments

8. Applicant's arguments filed May 4, 2007 have been fully considered but they are not persuasive.

102 rejection.

Applicant argues that Schuppan et al. fail to teach or suggest a method which encompasses the detection of antibodies against human tissue transglutaminase and at least one other transglutaminase molecule selected from group consisting of FXIIIA, TGk, transglutaminase X TGx, TGe and Band 4.2. This is not found persuasive because of reasons of record and further as stated above.

Applicant further argues that the antibodies of Schuppan et al would not necessarily "be cross reactive with other antigens," i.e., such as those encompassed by the present invention. Applicant states that none of the transglutaiminases (i.e., TGk, TGx, TGe) encompassed by the present methods are homologous to human tissue transglutamnase. Therefore, there is no factual to suggest that the antibodies of Schuppan et al would cross-react with TGk, TGx, TGe, nor is there basis to suggest that the antibodies of Schuppan et al would cross-react with FXIIIA or Band 4.2. This is not found persuasive because Schuppan et al specifically teaches at col 3, lines 49-52 that

the a-subunit of Factor XIII has a high degree of protein homology. Further, the antibodies to be detected are the same as the antibodies detected by applicant (IgA) (see specification). Thus, the antibodies of Schuppan et al would be cross reactive with other antigens and would inherently be against TGe. As shown by Applicant the IgA antibodies are cross reactive . The specification on page 15 discloses "the results shown support that serum IgA antibodes from patients with CD and DH react with both human TGc and TGe and further discloses that the serum antibodies from patients with CD and DH is directed against epitopes which are shared by the two transglutaminases". Further, the patients diagnosed in Schuppan et al have celiac disease and as stated by applicant on page 15, lines 12-13, serum IgA antibodies from patients with CD (celiac disease, same as disclose by Schuppan) react with both human TGc and TGe. Thus, it is inherent that the IgA antibodies of Schuppan et al are against both human tissue transglutaminase and TGe. Further, as stated above the body of the claim merely requires a step of taking a sample and testing the sample for IgA antibodies against human tissue transglutaminase and at least one other transglutaminase molecule. Further, since Schuppan et al is detecting the same antibodies as applicant in the same disease patients as applicant and since applicant shows that these antibodies are cross reactive one skilled in the art would envision that the antibody would be against other transglutamnases as recited. Further, the Patent and Trademark Office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference, in the first place between the antibodies of Schuppan et al and those instantly disclosed and, that if there

is such a difference, that such a difference would have been considered unexpected, i.e. unobvious by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430(CCPA 1977).

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit 1641
July 12, 2007

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